REMARKS

In response to the Office Action mailed April 18, 2008, Claims 1-15 and 17-27 stand pending and examined. The Examiner has rejoined previously withdrawn Claim 15. As Claim 15 has been rejoined, the status for Claim 15 now reflects "original".

A. 35 USC 112, 2nd paragraph

1. Claims 1-14 and 17-27 stand rejected for alleged indefiniteness under 35 USC 112, second paragraph with regard to the term "femtomolar". The Examiner contends that "femtomolar" does not specify a specific amount/range. Applicants respectfully traverse and overcome this rejection.

First, Applicants note that the term "femtomolar" is described and defined within paragraph 29 of the specification, with a specific detailed range of about 16 to about 320 femtomoles further defined. Claims 1, 13, 14 and 27, as previously amended (see April 9, 2007 response to the January 5, 2007 office action), reflect this defined and definite femtomolar range. As the other claims in this rejection depend upon base claims 1, 13 and 14, Applicants respectfully submit that the term "femtomolar" is described and distinctly defined, with a specific detailed range, in Claims 1-14 and 17-27.

Second, Applicants respectfully note that the Examiner has previously made this exact same rejection in the January 5, 2007 Office Action and subsequently **acknowledged** that the amendments to Claims 1, 13, 14 and 27 in Applicants' response of April 9, 2007 obviated the "femtomolar" indefiniteness rejection. In other words, the Examiner withdrew that the femtomolar indefiniteness rejection.

Accordingly, Applicants respectfully submit that the 112, second paragraph rejection has been obviated and therefore should be withdrawn.

B. 35 USC 103(a)

1. Claims 1-2, 7-12, 14-15, 19, 20 and 23-26 stand rejected under 35 USC 103(a) as allegedly anticipated by Kalbacher et al (J. Chromatography [1991] 548:343-350). Applicants respectfully traverse and overcome this rejection.

Kalbacher is asserted to teach isolation of antigenic peptides from human HLA-DR MHC class II molecules in femtomolar amounts via elution of a HLA-DR molecule-synthetic influenza peptide matrix after immunoaffinity purification, subsequent ultrafiltration, and then co-incubation with the potential antigenic peptides and subsequent acid elution of the HLA-DR molecules. The Examiner acknowledges that Kalbacher fails to teach concentration of the eluate, but that one of ordinary skill in the art would be able to elute at a wide range of concentrations. Applicants respectfully traverse.

Applicants note that the method of Kalbacher more specifically allegedly discloses the isolation of HLA-DR molecules which are then contacted with synthetic influenza matrix peptides. The HLA-DR molecules are purified with immunoaffinity and then eluted. Subsequently the buffer and detergent were exchanged by ultrafiltration. The isolated HLA-DR molecules are then co-incubated with potential antigenic peptides and the peptides bounded by the HLA_DR molecules are then isolated with addition of acid. Therefore Kalbacher requires and teaches a first elution of the HLA-DR molecule-synthetic matrix peptide complex and then, after ultrafiltration and co-incubation, requires and teaches a second elution wherein the potential antigenic peptides are eluted from the molecules via acid.

In contrast, Applicant's method only requires **one** elution step and additionally comprises a washing step of the sequestered peptide receptor (MHC class II molecule)-antigenic peptide beaded complex. Kalbacher does not teach nor disclose this method, but instead teaches away from Applicants claimed invention, as Kalbacher requires two elution steps and does not provide a washing of the beaded peptide receptor-antigenic

peptide complex. Furthermore, the Examiner acknowledges that Kalbacher fails to teach concentration of the eluate in both of its elution steps. Finally, Kalbacher provides no motivation nor suggestion for eliminating one elution step and then adding a washing of the beaded peptide receptor-antigenic peptide complex. Accordingly, Applicants respectfully submit that Kalbacher does not anticipate, nor render obvious, Applicants claimed invention.

Applicants therefore respectfully submit that the 103(a) rejection has been overcome and that said rejection as to claims 1-2, 7-12, 14-15, 19, 20 and 23-26, as amended, should be withdrawn and said claims put into condition for allowance.

2. Claims 1-3, 7-12, 14-15, 19, 20 and 23-26 stand rejected under 35 USC 103(a) as allegedly anticipated by Chicz et al (J. Exp. Med. [1993] 178:27-47). Applicants respectfully traverse and overcome this rejection.

Chicz is alleged to teach the isolation of antigenic peptides from human HLA-DR MHC class II molecules involving, inter alia, elution of the peptide-molecule complex via immunoaffinity precipitation and a subsequent elution of the peptides with acid (10% acetic acid). It is unclear how the Examiner alleges how Chicz renders Applicants claimed method obvious, as the Examiner subsequently cites Kalbacher et al. Regardless, Applicants respectfully traverse and overcome the Chicz 103(a) rejection.

Applicants first point out that Chicz et al allegedly discloses a method comprising immunoaffinity purifying the complexes, a first elution step of eluting the complexes, followed by concentrating and washing the complexes, and then a second elution step, wherein the antigenic peptides are eluted with 10% acetic acid, followed by subsequent washing and concentrating the peptides again. Chicz, like Kalbacher, thus requires two elution steps. Applicants' claimed invention only requires one elution step.

Additionally, Chicz does not teach isolating antigenic peptides in femtomolar amounts, much less the defined and definite range of Applicants claim 1. Indeed, the method of Chicz requires the presence of 1 mg of protein in order to get enough peptides for sequencing. Applicants' method of Claims 1 and 2 in contrast is an amount of 0.1 to 5 µg. The method of Chicz thus requires more starting material; the method of Applicants' invention has a much lower material loss and therefore allows a much smaller amount to start with.

Finally Chicz does not teach nor suggest nor motivate one of ordinary skill in the art to eliminate one elution step; nor which step to eliminate. Chicz also fails to teach suggest or motivate one of ordinary skill in the art to use less starting material to obtain peptides for sequencing.

Accordingly, Applicants respectfully submit that Chicz does not anticipate, nor render obvious, Applicants claimed invention. Applicants therefore respectfully submit that the 103(a) rejection has been overcome and that said rejection as to claims 1-3, 7-12, 14-15, 19, 20 and 23-26, as amended, should be withdrawn and said claims put into condition for allowance.

3. Claims 4, 17 and 18 stand rejected under 35 USC 103(a) as being unpatentable over Chicz et al (J. Exp. Med. [1993] 178:27-47) as applied to claims 2 and 16 above and further in view of Arndt et al (EMBO J. [2000] 19(6):1241-1251). Applicants respectfully traverse and overcome this rejection.

Chicz is alleged to disclose a general method for eluting and identifying peptide antigens from MHC Class II cells. The Examiner acknowledges that Chicz does not teach dendritic cells. Arndt is alleged to teach immunopurification of peptide-containing MHC Class II complexes from dendritic cells. The Examiner alleges it would have been obvious to use the dendritic cells of Arndt in the method of Chicz. Applicants respectfully traverse.

As discussed above, Chicz et al allegedly discloses a method comprising immunoaffinity purifying the complexes, a first elution step of eluting the complexes, followed by concentrating and washing the complexes, and then a second elution step, wherein the antigenic peptides are eluted with 10% acetic acid, followed by subsequent washing and concentrating the peptides again. Chicz thus requires two elution steps. Applicants' claimed invention only requires one elution step.

The addition of Arndt does not remedy the teaching of Chicz. Indeed, Arndt disclose the immunoprecipitation of complexes from B cells, washing with washing buffer and eluting the complexes. The antigenic peptides of Arndt are not eluted. Thus, Arndt requires the first elution step of Chicz but not the second elution step. Applicants' invention has only one elution step and that elution step involves the elution of the peptides. Arndt fails to teach Applicant's elution step. Arndt instead reinforces the first elution step of Chicz, which said elution is not a part of Applicant's invention.

Thus, even presuming *arguendo* that one had the motivation to combine Arndt with Chicz, the combined methodology would not disclose or teach Applicants' method. Accordingly, Applicants respectfully submit that the 103(a) rejection has been obviated and overcome and that said rejection as to claims 4, 17 and 18 should be withdrawn and said claims put into condition for allowance.

Applicants further respectfully note that the instant 103(a) rejection of Chicz in view of Arndt was withdrawn in light of Applicants amendments and response of April 9, 2007. Accordingly, Applicants respectfully submit that the 103(a) rejection has been previously obviated and overcome and that said rejection as to claims 4, 17 and 18 should be withdrawn and said claims put into condition for allowance.

No further fee is required in connection the filing of this Amendment. If any additional fees are deemed necessary, authorization is given to charge the amount of any such fee to Deposit Account No. 08-2525.

Respectfully submitted,

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